

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

MINERAL OIL – **KEROSENE**

Chemical Code # 002071 & 401, Tolerance # 00149, SB 950 # 721 & 754

Original date: 12/14/01

I. DATA GAP STATUS

Chronic, rat:	Data gap, no study on file
Chronic, dog:	Data gap, no study on file
Combined (Chronic/onco), mouse:	Data gap, inadequate study, possible adverse effect indicated
Oncogenicity, rat:	Data gap, no study on file
Reproduction, rat:	Data gap, no study on file
Teratology, rat:	Data gap, inadequate study, no adverse effects indicated.
Teratology, rabbit:	Data gap, no study on file
Gene mutation:	Data gap, inadequate study, possible adverse effects indicated.
Chromosomal aberration:	No data gap, possible adverse effect indicated
DNA damage:	Data gap, no study on file
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T010719

Original: J. Gee, 11/2/87; Revised: M. Silva, 9/88; Kishiyama & Silva, 12/14/01

Kerosene one-liners and worksheets are from studies filed under MINERAL OIL (Chemical Code #: 401, SB 950#: 754, DPN#: 149). Kerosene also has DPN #: 149 but the chemical code is 2071

and the SB950 number is 721.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

No study submitted

CHRONIC TOXICITY, RAT

Subchronic:

149 - 016 117305 "Four Week Subchronic Inhalation Toxicity Study in Rats," (Ulrich, C.E.; International Research and Development Corporation, Mattawan, MI; IRDC Study 418-027; 6/28/86. API #81-07, API #81-09, and API #81-10 each at a concentration of 25 mg/m³ were administered via whole body inhalation exposure 6 hours/day, 5 days/week for 4 weeks to 20 Charles River CD7 rats/sex/group. Treatment related effects were: increased leukocytes (29 & 31%) and lymphocytes (21 & 32%) for API #81-10 treated males and females. An increased incidence in subacute inflammation of the respiratory mucosa occurred with the API #81-09 treatment. UNACCEPTABLE (not a FIFRA Guideline study). These data are supplemental. (Kishiyama & Silva, 5/18/01).

CHRONIC TOXICITY, DOG

No study submitted

ONCOGENICITY, RAT

No study submitted

COMBINED, MOUSE

149 - 019 117313 "Lifetime Dermal Carcinogenesis/Chronic Toxicity Screening Bioassay of Refinery Streams in C₃H/HeJ Mice," (Dennis, M.W.; Primate Research Institute, PRI Study No: AP-135r; 10/3/86). Twelve petroleum refinery streams (API #81-03, API #81-07 to 10, API #81-13 to 15, API #81-24, API #83-01 to 03) were evaluated for possible chronic toxicity (12 months) and carcinogenicity (24 months). Compounds were administered dermally undiluted (50 µl) twice/week to C₃H/HeJ male mice (50/group) for 12-24 months. Dermatotoxic effects were reported for all test materials. **Refinery streams were ranked as "strong": API #81-15; "intermediate": API #81-07, API #81-09, API #81-10, API #83-02; API #83-03 or "weak": API #81-03, API #83-01 in carcinogenic effect.** Possible adverse effect. Not acceptable and not upgradeable. There were major deficiencies and the study was not performed according to FIFRA Guidelines. (Kishiyama & Silva, 11/7/00).

REPRODUCTION, RAT

No study submitted

TERATOLOGY, RAT

149 - 020 117322 “A Teratology Study in Rats (Kerosene),” (Beliles, R.P.; Litton Bionetics, Inc., LBI Project No. 20698-10; 3/79). Kerosene was administered in air (as a vapor) to mated CRL:COBS CD (SD) BR rats (20/dose) at 0, 106.4 and 364.0 ppm (6 hours/day) during gestation days (gd) 6 through 15. Maternal NOEL <364.0 ppm. Developmental NOEL > 364.0 ppm. There were no treatment-related effects (maternal or fetal) at any dose. This study is not acceptable and not upgradeable, due to lack of an MTD, as well as numerous deficiencies (no dose selection rationale not reported; should be 3 test levels, no individual maternal data). No adverse effects indicated, however there was no MTD. These data are supplemental. (Kishiyama & Silva, 12/27/00).

TERATOLOGY, RABBIT

No study submitted

GENE MUTATION

149 - 022 117339A “Mutagenicity Evaluation of Kerosene,” (Brusick, D.J.; Litton Bionetics, Inc., LBI Project #: 2697; 3/77). Kerosene was tested at 0, 0.001-5.0 µl/plate and 0.625% - 5% (+/- S9) using *Salmonella typhimurium* strains (TA1535, TA1537, TA1538, TA98, TA100) and *Saccharomyces cerevisiae* (D4) by plate overlay and suspension methods. Mouse lymphoma cells were used at 0.008 - 0.130 µl/ml and 0.004 - 0.065 µl/ml (+/- S9) to evaluate mutagenicity. No mutagenic activity was observed with kerosene in the three tests. Not acceptable and not upgradeable. No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 4/25/01).

149 - 022 117338A “Mutagenicity Evaluation of Hydrodesulfurized Kerosene (API #81-07) in the Mouse Lymphoma Forward Mutation,” (Cifone, M.A.; Litton Bionetics, Inc., Kensington, MD; Project PS-4-LBI (503-1); API Medical Research Publication: 32-30240; 12/4/84). API# 81-07 technical (100% pure) at 0, 6.25, 12.5, 25.0 and 37.5 nl (no S9) and at 0, 3.91, 7.81, 15.6, 31.3 and 62.5 nl/ml (+ S9) was evaluated for mutagenicity using mouse lymphomas. There were no treatment-related effects either with or without S9 at any dose. This study is incomplete, is not acceptable and is not upgradeable. The data are supplemental. (Kishiyama & Silva, 4/24/01).

149 - 022 117340 “L5178Y TK+/- Mouse Lymphoma Mutagenesis Assay of API 83-09,” (Rogers-Back, A.; Microbiological Associates, Inc., Study No. T2460.701; 10/10/85). API 83-09 at 0.01 to 0.21 µl/ml (no S9) and at 0.0067 to 0.21 µl/ml (+S9) was evaluated for mutagenicity (1-3 replicates/dose) using mouse lymphoma cells (L5178Y TK+/-). **Mutation frequency was significantly increased as follows: No S9 = 2 - 13 times (0.056 & 0.042 µl/ml), 3 - 8 times (0.021 - 0.067 µl/ml) and 2 times (0.032 µl/ml) in Tests #1, 2 and 4 respectively; +S9 = 3.5 times (0.21 µl/ml) in Test #2. UNACCEPTABLE (no individual data, copy of report is not of good quality).** (Kishiyama & Silva, 4/27/01).

149 - 022 117339 “Mutagenicity Evaluation of Kerosene,” (Brusick, D.J.; Litton Bionetics, Inc., LBI Project #: 2697; 3/77). Kerosene was tested at 0, 0.001-5.0 µl/plate and 0.625% - 5% (+/- S9) using *Salmonella typhimurium* strains (TA1535, TA1537, TA1538, TA98, TA100) and *Saccharomyces cerevisiae* (D4) by plate overlay and suspension methods. Mouse lymphoma cells were used at 0.008 - 0.130 µl/ml and 0.004 - 0.065 µl/ml (+/- S9) to evaluate mutagenicity. No mutagenic activity was observed

with kerosene in the three tests. Not acceptable and not upgradeable. No adverse effect indicated. These data are supplemental. (Kishiyama & Silva, 4/25/01).

CHROMOSOMAL ABERRATION

****149 - 021 117333** “The Acute *In Vivo* Cytogenetics Assay in Male and Female Rats of API Sample 83-09,” (Putman, D.L.; Microbiological Associates, Inc., Bethesda, MD; Testing Facility Number: MA Study No. T2460.105001; 5/4/85). API-83-09 was administered to Sprague-Dawley rats (5/sex/dose/time point) as a single IP injection at 0.3, 1.0 and 3.0 gm/kg. Bone marrow cells, arrested in metaphase were collected at 6, 24, and 48 hours after treatment. API 83-09 treatments did not significantly increase the number of cells with aberrations or the number of aberrations per cell in this study. ACCEPTABLE No adverse effect. (Kishiyama & Silva, 5/4/01).

**** 149 - 022 117338B** “Mutagenicity Evaluation of Hydrodesulfurized Kerosene (API #81-07) in the Rat Bone Marrow Cytogenetic Assay,” (Cimino, M.C.; Litton Bionetics, Inc., Kensington, MD; Project PS-4-LBI (503-1); LBI Project #: 22162 & 20989; 11/84). API# 81-07 (purity not designated) was administered via a single intraperitoneal injection to Sprague-Dawley rats (5/sex/dose/sacrifice time + 5/sex supplementary group at high dose) at 0, 0.3, 1.0 or 3.0 g/kg/day (6, 24 & 48 hour sacrifice) to evaluate induction of structural aberration in bone marrow cells (50 metaphases/animal; 500 cells counted/animal for mitotic index). High dose animals had mortality, nervous depression and were febrile to the touch. The positive control (TEM) was the only group reported with a significant increase of structural chromosome aberration. No adverse effect. ACCEPTABLE. (Kishiyama & Silva, 4/13/01).

149 - 022 117339B “Mutagenicity Evaluation of Kerosene” (Brusick, D.J.; Litton Bionetics, Inc., Kensington, MD; LBI Project No. 2697; 3/77). Kerosene administered *via* a single I.P. injection at 0, 0.04, 0.13 and 0.40 ml/rat (males) in an acute study and once daily for 5 days at 0, 0.02, 0.06 and 0.18 ml/rat (male) in a subchronic study. Sacrifice was scheduled for 5 males/group at 6, 24 and 48 hours (acute study) and at 6 hours after the final injection (subchronic study). Structural chromosome aberrations did not increase significantly relative to the control (acetone) for all treatments (including the positive control). UNACCEPTABLE. Not upgradeable (Fifty suitable metaphases were not located for many of the animals). There were insufficient data to determine a possible adverse effect. These data are supplemental. (Kishiyama & Silva, 4/26/01).

149 - 022 117342 “*In Vivo* Chromatid Exchange Assay with API 81-07 Hydrodesulfurized Kerosine,” (Putman, D.L.; Microbiological Associates, Inc., Bethesda, MD; Lab. Study No. T5337.130002; 9/26/88). API 81-07 was administered to B6C3F1 mice (5/sex/dose) in a single IP injection at 400, 2000 or 4000 mg/kg. Bone marrow from the femurs was collected 24-26 hours after treatment. Body weight was slightly reduced for high dose males and females and mid dose males. **Adverse effect: SCE/metaphase in males was significantly increased at all three concentrations (400, 2000, 4000 mg/kg) of API 81-07 tested.** NOEL for female > 4000 mg/kg (No increase in SCE at any dose.) NOEL for male = <400 mg/kg (Significantly increased SCE at all doses but not dose-related.) UNACCEPTABLE (low dose not low enough; dosing material analysis to confirm concentration and stability is not reported; no individual data). Possible adverse effect indicated. Supplemental data. (Kishiyama & Silva, 4/30/01)

****149 - 022 117337** “Sister Chromatid Exchange Assay in Chinese Hamster Ovary (CHO) Cell with API 81-07 Hydrodesulfurized Kerosine,” (Putman, D.L.; Microbiological Associates, Inc.; Laboratory

Study #: T5337.334006; 10/88). API -81-07 (purity not provided) was used on Chinese hamster ovary cells (CHO) at 0, 0.007, 0.013, 0.025 and 0.05 µl/ml (no S9) and at 0, 0.05, 0.1, 0.2 and 0.4 µl/ml (+S9) for induction of sister chromatid exchange (SCE). There was no significant treatment-related increase in SCEs. Positive controls behaved as expected. ACCEPTABLE. No adverse effect. (Kishiyama & Silva, 4/12/01)

DNA DAMAGE

No study submitted.

NEUROTOXICITY

Not required at this time.

SUPPLEMENTAL STUDIES

149 – 016 117304 “Petroleum Hydrocarbon Toxicity Studies: XI. Animal and Human Response to Vapors of Deodorized Kerosene,” (Carpenter, C.P., Geary, Jr., D.L., Myers, C., Nachreiner, D.J., Sullivan, L. J., King, J.M.; Carnegie-Mellon Research Institute, Carnegie-Mellon University, Pittsburgh, PA; 12/22/75; Published in: Toxicology and Applied Pharmacology, 36:443-456, 1976). **Acute Study:** Deodorized Kerosene (composed of paraffins, naphthenes, aromatics; boiling point temperature range: 406 – 522 °F) was administered by inhalation (air saturated at 25 °C) to 6 male albino rats for 8 hours, during which time the rats appeared normal. There were no effects on weight gain during the 14 day post-dosing observation period, nor were there effects at autopsy. 6 Rats were then exposed at 0, 6.9, 7.0, 7.4 and 9.6 mg/liter (ave/day for 4 days) for 6 hr/day. After exposure, the extremities of the rats were red, but coordination was normal (sluggish after 3 hours). 1 day after termination of treatment, rat skin was dry and flakes formed. This effect continued for 4 days and 1/6 rats had hair loss. Body weight gain was similar between treated and control rats. No increase in osmotic-erythrocyte fragility was observed among 6 rats treated at 5.9 mg/L for 6 hours (compared to controls). Mixed breed cats (4 males) were exposed by aerosol inhalation (6.4 mg/L) for 6 hours. No treatment-related effects were observed during treatment or at autopsy. 6 Mice, treated with the highest attainable vapor concentration, were not affected. They were then treated with an aerosol of Deoderized Kerosene at 6.9 mg/L (6900 mg/m³) for upper respiratory irritation. The respiratory rates of the mice were not depressed 50% or more from control values. Neither saturated vapor generated at room temperature nor the above aerosol were irritating to the upper respiratory tracts of mice. **Subacute Inhalation Toxicity:** Rats (25 males/dose) and Beagle dogs (3 males/dose) received repeated daily inhalation exposure (6 hours/day, 5 days/week) to 0, 0.02, 0.048 and 0.10 mg/liter for 3, 8 and 13 weeks. iced for histopathology after 16 and 40-day intervals. Results showed no treatment-related effects in any of the monitored criteria (hematology, blood chemistry, body weight, histopathology when inhaled for 67 and 68 days by rats and dogs, respectively). **Human Sensory Response:** Odor threshold was measured on 6 volunteers (age 23-49) were exposed at 0.01, 0.001, 0.00, and 0.1 mg/L for 10 seconds Day 1, and 0.1, 0.01, 0.00 and 0.001 mg/L on day 2. The odor threshold was between 0.0002 and 0.002 mg/L. 6 Volunteers (age 20-63) inhaled a mean measured vapor:air concentration of 0.14 mg/L for 15 min. There was no discomfort or irritation during or following the inhalation period. A 15 min exposure to vapor:air concentration of 0.14 mg/L of Deoderized kerosene would be acceptable for an 8 hour work day. These data are supplemental. M. Silva, 5/17/01.